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ORIGINAL ARTICLE

The Clinical and Economic Impact of Measles-Mumps-Rubella Vaccinations to Prevent Measles Importations From US Pediatric Travelers Returning From Abroad

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Background. Pediatric international travelers account for nearly half of measles importations in the United States. Over one third of pediatric international travelers depart the United States without the recommended measles-mumps-rubella (MMR) vaccinations: 2 doses for travelers ≥12 months and 1 dose for travelers 6 to <12 months.

Methods. We developed a model to compare 2 strategies among a simulated cohort of international travelers (6 months to <6 years): (1) *No pretravel health encounter (PHE):* travelers depart with baseline MMR vaccination status; (2) *PHE:* MMR-eligible travelers are offered vaccination. All pediatric travelers experience a destination-specific risk of measles exposure (mean, 30 exposures/million travelers). If exposed to measles, travelers' age and MMR vaccination status determine the risk of infection (range, 3%-90%). We included costs of medical care, contact tracing, and lost wages from the societal perspective. We varied inputs in sensitivity analyses. Model outcomes included projected measles cases, costs, and incremental cost-effectiveness ratios ($/quality-adjusted life year [QALY], cost-effectiveness threshold ≤$100 000/QALY).

Results. Compared with no PHE, PHE would avert 57 measles cases at $9.2 million/QALY among infant travelers and 7 measles cases at $15.0 million/QALY among preschool-aged travelers. Clinical benefits of PHE would be greatest for infants but cost-effective only for travelers to destinations with higher risk for measles exposure (ie, ≥160 exposures/million travelers) or if more US-acquired cases resulted from an infected traveler, such as in communities with limited MMR coverage.

Conclusions. Pretravel MMR vaccination provides the greatest clinical benefit for infant travelers and can be cost-effective before travel to destinations with high risk for measles exposure or from communities with low MMR vaccination coverage.

Key words. cost-effectiveness; measles; MMR; pediatrics; travel medicine.

Measles is a highly contagious viral illness characterized by fever, cough, coryza, conjunctivitis, and a distinctive maculopapular rash. Up to 40% of patients experience complications, including diarrhea, ear infection, pneumonia, and encephalitis [1, 2]. Young children are at high risk for severe illness or death [2, 3]. A single case of measles can result in multiple transmissions and is extremely costly to hospitals and public health systems where resources must be deployed to identify exposed individuals and limit potential spread [4]. High uptake of the measles-mumps-rubella (MMR) vaccine eliminated endemic measles transmission in 2000 in the United States [5]. However, US residents who travel internationally are at increased risk for measles exposure, and infections acquired abroad can result in domestic outbreaks [6].

The Advisory Committee on Immunization Practices (ACIP) recommends that all US children receive 1 dose of MMR vaccine between ages 12 and 15 months and a second dose between ages 4 and 6 years [7]. For children traveling internationally, ACIP recommends an altered schedule in which infants (6 to <12 months) receive 1 dose of MMR prior to departure, which does not count toward the 2 lifetime doses. Preschool-aged children (1 to <6 years) traveling should receive both lifetime doses prior to departure, at least 28 days apart [7, 8]. Previous research has shown that 63% of children ages 6 months to <6

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years attending pretravel clinics between 2009 and 2018 were eligible for MMR vaccination, yet only 45% received the recommended MMR vaccination(s) [9].

MMR vaccination of eligible pediatric travelers could reduce the number of measles cases imported into the United States, thus averting measles-related morbidity, mortality, and costs [10, 11]. Using a decision tree model, we projected the clinical and economic impact of pretravel health encounters to improve MMR vaccination among departing pediatric travelers ages 6 months to <6 years.

METHODS

Model Structure

We adapted a previously published decision tree (TreeAge, Williamstown MA) for MMR vaccination in travelers and compared 2 strategies among pediatric international travelers: (1) No pretravel health encounter (PHE) and (2) PHE [12]. Travelers in both strategies begin the simulation with an age-dependent "baseline vaccination status" of 0, 1, or 2 MMR vaccination(s). In the no PHE strategy (Supplementary Figure 1, top), all travelers depart with this baseline vaccination status. During travel, individuals have a destination-dependent risk of exposure to measles. If exposed, the risk of becoming infected with measles is stratified by age and vaccination status. Returning travelers infected with measles can transmit the infection to others in the community, resulting in US-acquired cases and necessitating contact tracing. In the PHE strategy (Supplementary Figure 1, bottom), providers evaluate travelers for baseline vaccination status and MMR vaccine eligibility; they offer vaccination based on ACIP recommendations [7]. Guardians can refuse vaccination. Model structure for travel-related measles exposure, illness, and transmission is the same in both strategies.

Input Parameters

Cohort Characteristics.

Data from Global TravEpiNet (GTEN), a consortium of 29 US clinical sites that prospectively collect data regarding pretravel advice, informed input parameters for a simulated cohort of pediatric travelers. Based on ACIP MMR recommendations, we considered 2 age groups: infant travelers (6 to <12 months; median, 10 months) and preschool-aged travelers (1 to <6 years; median, 3 years) (Table 1) [9]. Among infant travelers at baseline, 92% had no MMR vaccinations, 8% had 1 MMR vaccination, and none had 2 MMR vaccinations. Eight percent of preschool-aged travelers had no MMR vaccinations, 52% had 1 MMR vaccination, and 40% had 2 prior MMR vaccinations at baseline [9].

Risk of Measles Exposure.

We estimated the risk of exposure to measles virus while traveling abroad ($Risk_{exposure}$) from documented numbers of measles importations, the MMR vaccination status of infected travelers, and the overall number of US international travelers (Supplementary Methods, Supplementary Tables 1-6), We also calculated $Risk_{exposure}$ for specific destinations (Table 1).

Clinical Implications of Measles Exposure.

Travelers' risk of becoming infected depends on age and vaccination status at the time of measles exposure. We estimated that exposed preschool-aged travelers have a 3% chance of becoming infected with measles after 2 doses of MMR vaccine, and a 7% chance of becoming infected after 1 dose [1, 7]. We estimated that 15% of infants exposed to measles will be infected if they previously received 1 MMR dose. Unvaccinated travelers of any age have a 90% chance of infection after exposure [1, 7]. People with nonfatal measles infection incur a loss of 0.019 quality-adjusted life years (QALYs) and experience an age-stratified probability of measles-associated death (Table 1; Supplementary Methods) [13, 14].

US-acquired cases result when an infected traveler transmits measles virus to others upon returning to the United States. Based on Centers for Disease Control and Prevention (CDC) measles surveillance data (2009-2018), we assumed that each measles case importation from an unvaccinated (or partially vaccinated) pediatric traveler resulted in 4 US-acquired cases; travelers who received 2 lifetime doses of MMR vaccine did not transmit measles virus to others [17, 18].

All known measles cases require contact tracing [19]. We estimated that each imported measles case would lead to public health tracing of 1500 contacts [11], regardless of the traveler's vaccination status [20]. Because of variability in the reported number of contacts requiring tracing [11, 18, 21–24], we conducted extensive sensitivity analyses on this parameter.

Measles Infection and Public Health Costs.

We derived model input costs from the societal perspective, including direct medical costs, indirect costs of lost wages, and contact tracing [25]. We estimated direct medical costs for a measles case: $150 for outpatient care and $32 500 for hospitalization (Supplementary Methods, Supplementary Tables 7-8). For imported and US-acquired measles cases, we weighted these costs by the percentage of patients requiring hospitalization [26]. We estimated a total weighted-average cost of $13 900 for each imported case, including direct medical costs ($11 800) and the indirect cost of lost wages due to guardians missing work to care for a sick child ($2100) (Table 1; Supplementary Methods, Supplementary Tables 9-13). The total cost for a US-acquired case is $5600, including direct medical costs ($3800) and indirect missed work costs ($1800) (Supplementary Methods, Supplementary Tables 7, 8, and 11-13). Each contact incurs a cost of $570, including the cost to public health departments for tracing ($330) and missed work for the contact or contact's guardian ($240) (Supplementary Methods, Supplementary Tables 9-13).

Table 1. Base Case Input Parameters for a Decision Tree Model Assessing the Clinical Impact and Cost-Effectiveness of MMR Vaccination during a Pretravel Health Encounter for Infant and Preschool-Aged Travelers

Variable	Base Case		Source
Cohort characteristics			
Demographics	Infants	Preschool-aged	GTEN [9]
Median age (IQR)	10 mo (8-10 mo)	3 yr (2-4 yr)	
Female (%)	52	48	
Baseline MMR vaccination status (% of travelers)			GTEN [9]
Two MMR vaccinations	0	40	
One MMR vaccination	8	52	
Zero MMR vaccinations	92	8	
Risk of measles exposure during travel (exposures per million travelers)			See Supplementary Methods
	All pediatric travelers		
All international travel	30		
Travel to the Americas[a]	2		
Overseas travel[a]	93		
By continent			
Travel to North America	2		
Travel to South America	3		
Travel to Europe	46		
Travel to Africa	145		
Travel to Asia	151		
Risk of measles infection, if exposed (%)	Infants	Preschool-aged	CDC, ACIP [1, 7]
Two MMR vaccinations	—	3	
One MMR vaccination	15	7	
Zero MMR vaccinations	90	90	
US-acquired cases, if infected (n)	All pediatric travelers		CDC [Unpublished data]
Two MMR vaccinations	0		
One MMR vaccination	4		
Zero MMR vaccinations	4		
Contacts, if infected (n)	1500		Ortega-Sanchez et al [11]
QALYs lost per nonfatal measles infection	0.019		Thorrington et al [13]
Probability of death, if infected			Perry and Halsey [14]
<5 yr	0.0034		
5-9 yr	0.0014		
10-19 yr	0.0001		
20-29 yr	0.0028		
>30 yr	0.0066		
Costs of measles infection (USD)[b]			See Supplementary Methods
Per imported measles case	$13 900		See Supplementary Methods
Per US-acquired measles case	$5600		See Supplementary Methods
Per contact, public health tracing	$330		Ortega-Sanchez et al [11]
Per contact, missed work[c]	$240		See Supplementary Methods
Pretravel health encounter (PHE)	Infants	Preschool-aged	See Supplementary Methods
Probability of MMR vaccination (%)	57	44	GTEN [9]
Cost of PHE[d]	$8.30	$8.30	See Supplementary Methods
Cost of vaccination (USD)	$96	N/A	CMS, CDC [15, 16]

All costs are reported in 2018 USD.

Abbreviations: ACIP, Advisory Committee on Immunization Practices; MMR, measles-mumps-rubella; IQR, interquartile range; mo, months; yr, years; GTEN, Global TravEpiNet; NTTO, National Travel and Tourism Office; CDC, Centers for Disease Control and Prevention; CMS, Centers for Medicare and Medicaid Services; USD, US dollars; QALY, quality-adjusted life year; PHE, pretravel health encounter.

[a]Travel to the Americas includes North and South America, while overseas travel includes travel to Africa, Asia, and Europe and excludes travel in the Americas.

[b]Costs of measles infection include direct costs of medical care and indirect cost associated with missing lost wages due to missed work for guardians.

[c]Assumes 8 h of missed work per contact, assuming some contacts have evidence of previous vaccination, while other susceptible contacts may be recommended to quarantine or pursue post-exposure prophylaxis (see Supplementary Methods).

[d]Visit cost is pro-rated 3% for time during PHE spent on evaluation of measles immunity and recommendation regarding MMR vaccination.

Pretravel Health Encounter.

Of those eligible for MMR vaccination based on age and baseline vaccination status, 57% of infant travelers and 44% of preschool-aged travelers receive the ACIP-recommended MMR vaccination (Table 1) [9]. All travelers in the PHE strategy incur a cost of $8.20, including a $6 visit cost and a $2.20 missed work

cost, both pro-rated at 3% for the amount of visit time spent on measles (Supplementary Tables 14-17). Because the early MMR dose recommended by ACIP guidelines for infant travelers does not count toward the 2 lifetime doses given after 12 months of age, we included the cost of MMR vaccination in the PHE strategy for infant travelers [15, 16]. We did not include the costs of MMR vaccine or its administration for preschool-aged travelers, who should receive vaccination regardless of travel plans because 2 doses of MMR vaccine are recommended for children ≥12 months [7].

Model Outcomes

Model outcomes included the number of imported and US-acquired measles cases, QALYs, and costs. We report the incremental cost-effectiveness ratios (ICER, $/QALY) over a lifetime based on 3% discounted results [25]. We considered the following cost-effectiveness thresholds: ≤$50 000/QALY, ≤$100 000/QALY, and ≤$200 000/QALY [25, 27]. PHE was cost-saving if it resulted in better clinical outcomes and was less costly than no PHE.

Sensitivity and Scenario Analyses

We performed 1-way sensitivity analyses by varying all clinical (eg, number of US-acquired cases resulting from an importation) and cost parameters (eg, medical care costs for measles infection) [28]. We determined thresholds at which PHE became cost-effective or cost-saving. We examined 2-way sensitivity analyses with $Risk_{exposure}$ with the number of US-acquired cases per imported measles case, PHE costs, and the probability of vaccination at PHE. In scenario analyses, we investigated the impact of averting measles importations into US communities with lower MMR vaccination coverage [29, 30], using data from past measles outbreaks (Supplemental Methods) [10, 21–24].

RESULTS

Base Case

In a simulated cohort of 1 million US infant travelers, no PHE would result in 25 imported measles cases and 99 US-acquired cases and cost $22.1 million (Table 2, top). PHE would result in 13 imported measles cases and 54 US-acquired cases and cost $69.6 million. Compared with no PHE, PHE would avert 57 measles cases (or 5 discounted QALYs gained) at an additional cost of $47.5 million (ICER, $831 000/measles cases averted or $9.2 million/QALY).

In an equal-sized cohort of US preschool-aged travelers, no PHE would result in fewer imported (4) and US-acquired (13) measles cases at a lower cost ($3.2 million) than infant travelers (Table 2, bottom). PHE would reduce the number of measles cases to 2 imported and 7 US-acquired cases at a cost of $12.5 million, thus averting 7 measles cases (or 1 discounted QALY gained) at a cost of $9.3 million (ICER, $15.0 million/QALY).

Destination-Specific Risk of Measles Exposure

Results varied widely by destination and age group (Table 2). For infant travelers to Asia or Africa, PHE would result in $20 000 or $28 000/measles case averted, respectively, but would remain above the $200 000/QALY cost-effectiveness threshold.

Threshold Analyses

In 1-way sensitivity analyses, PHE would be cost-effective at the $100 000/QALY threshold for infant travelers when: $Risk_{exposure}$ was ≥160 exposures/million travelers; PHE direct costs were reduced by ≥85%; or ≥8720 contacts required public health tracing. PHE would be cost-saving when: $Risk_{exposure}$ ≥168 exposures/million travelers; PHE direct costs were ≥86% reduced; or ≥8800 contacts. PHE would be cost-effective for preschool-aged travelers only when $Risk_{exposure}$ was ≥269 exposures/million travelers. PHE offers a lower value if the probability of death from measles is only 1.4 deaths/1000 cases (Supplementary Table 19) [26].

Two-Way Sensitivity Analyses

$Risk_{exposure}$ and US-Acquired Cases.

At the $100 000/QALY threshold, PHE would be cost-effective for infant travelers to Asia and Africa if at least 8 or 11 US-acquired cases occurred, respectively, or for infants traveling Overseas if ≥53 US-acquired cases resulted (Figure 1A). PHE would be cost-saving for infants when ≥22 (≥29) US-acquired cases occurred after travel to Asia (Africa).

For preschool-aged travelers, PHE would be cost-effective at the $100 000/QALY threshold if ≥49 (53) US-acquired cases occurred after travel to Asia (Africa) (Figure 1B).

$Risk_{exposure}$ and PHE Costs.

PHE became cost-saving for infant travelers when PHE direct costs were reduced by 11% for travelers to Asia, 15% (Africa), 47% (Overseas), or 76% (Europe) (Figure 2A) or when indirect costs increased by 31% (Asia) and 43% (Africa) (Figure 2B).

$Risk_{exposure}$ and Probability of Vaccination at PHE.

PHE was cost-effective at the $100 000/QALY threshold when ≥90% of eligible infant travelers to Asia or 100% of eligible preschool-aged travelers to Asia were vaccinated at PHE (Supplementary Figure 2).

Scenario Analysis

Among pediatric travelers to Europe or Asia, PHE demonstrated the best value for travelers returning to communities with low MMR vaccination coverage (ie, more US-acquired cases and contacts resulting from 1 imported measles case).

Table 2. Base Case Results for a Decision Tree Model Assessing the Clinical Impact and Cost-Effectiveness of MMR Vaccination During a Pretravel Health Encounter for Infant and Preschool-Aged Travelers, Per Million US Travelers

	Imported Measles Cases	US-Acquired Measles Cases	Averted Measles Cases	QALYs Gained (Undiscounted)	QALYs Gained (Discounted) [a]	Cost (USD)[a]	ICER (USD/Measles Case Averted)[a]	ICER (USD/QALY)[a]
Infant travelers								
Any international travel ($Risk_{exposure}$ 30 exposures/1M travelers)								
No PHE	25	99				22 127 000		
PHE	13	54	57	12	5	69 585 000	831 000	9.2M
Overseas[b] ($Risk_{exposure}$ 93 exposures/1M travelers)								
No PHE	78	313				69 595 000		
PHE	42	169	180	38	16	95 222 000	143 000	1.6M
Europe ($Risk_{exposure}$ 46 exposures/1M travelers)								
No PHE	38	153				34 162 000		
PHE	21	83	88	19	8	76 085 000	475 000	5.3M
Africa ($Risk_{exposure}$ 145 exposures/1M travelers)								
No PHE	122	487				108 392 000		
PHE	66	263	280	60	25	116 176 000	28 000	309 000
Asia ($Risk_{exposure}$ 151 exposures/1M travelers)								
No PHE	127	507				112 878 000		
PHE	68	274	291	62	26	118 598 000	20 000	218 000
Preschool-aged travelers								
Any international travel ($Risk_{exposure}$ 30 exposures/1M travelers)								
No PHE	4	13				3 233 000		
PHE	2	7	7	2	1	12 537 000	1.3M	15.0M
Overseas[b] ($Risk_{exposure}$ 93 exposures/1M travelers)								
No PHE	11	41				10 169 000		
PHE	8	23	22	5	2	17 149 000	317 000	3.6M
Europe ($Risk_{exposure}$ 46 exposures/1M travelers)								
No PHE	6	20				4 992 000		
PHE	4	11	11	2	1	13 707 000	807 000	9.1M
Africa ($Risk_{exposure}$ 145 exposures/1M travelers)								
No PHE	18	64				15 838 000		
PHE	12	36	34	7	3	20 919 000	148 000	1.7M
Asia ($Risk_{exposure}$ 151 exposures/1M travelers)								
No PHE	19	67				16 493 000		
PHE	12	38	36	8	3	21 354 000	136 000	1.5M

Abbreviations: QALY, quality-adjusted life years; ICER, incremental cost-effectiveness ratio; USD, US dollars; $Risk_{exposure}$, risk of exposure to measles virus; PHE, pretravel health encounter; M, million; MMR, measles-mumps-rubella.

[a]QALYs and costs are discounted at 3%; ICERs are calculated with discounted results. Costs and ICERs are rounded to the nearest 1000.
[b]Overseas includes all international destinations outside of North and South America.

PHE was cost-saving for infants returning from Europe to communities in which more than 5500 contacts occurred per importation (Figure 3A) and cost-effective for preschool-aged travelers (at $100 000/QALY thresholds) in half of the simulated combinations of US-acquired cases and contacts (Figure 3C). The value of PHE for travelers to Asia was cost-saving if an infant or preschool-aged importation prompted >1500 contacts or >2500 contacts, respectively (Figure 3B and 3D).

DISCUSSION

Our model-based results demonstrate that a pretravel health encounter can provide a valuable opportunity to protect pediatric travelers from measles infection and reduce the number of measles cases in the United States. We find that pretravel MMR vaccination has the greatest clinical impact among infant travelers and can be cost-effective or cost-saving for infant travelers to Asia and Africa, especially for pediatric travelers returning to communities with low MMR vaccination coverage.

The risk of measles exposure while traveling abroad was the most important factor in determining the cost-effectiveness of MMR vaccination at pretravel health encounters. This risk may be rising for US travelers, even in places perceived as low-risk destinations, such as Europe [31]. Before disruptions in reporting due to the COVID-19 pandemic, worldwide measles incidence increased from 18 cases per million in 2016 to 120 per million in 2019 [32]. With travel resuming amidst disruptions

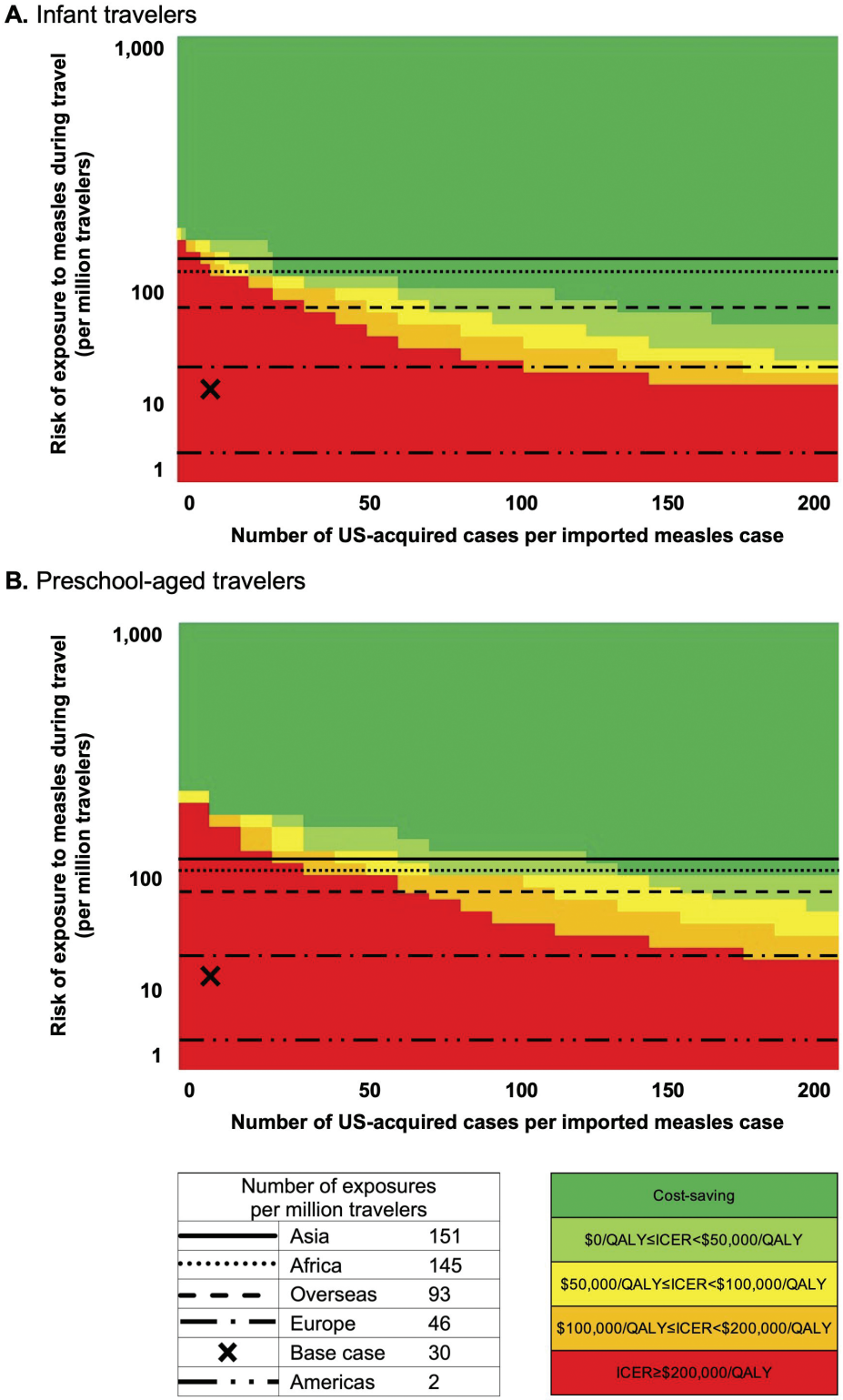


Figure 1. A 2-way sensitivity analysis depicts the value of PHE compared with no PHE when the risk of measles exposure and the number of US-acquired cases per imported measles case are varied simultaneously for infant travelers (A) and preschool-aged travelers (B). The 2 parameters examined in 2-way sensitivity analyses are the number of US-acquired cases per imported measles case (horizontal axis) and the risk of exposure to measles during travel (vertical axis). Dark green marks when PHE is both clinically and economically preferred to no PHE (cost-saving); light green marks the values at which the ICER of PHE compared with no PHE is ≤$50 000/QALY; yellow marks the values at which the ICER is >$50 000/QALY but ≤$100 000/QALY; orange marks the values at which the ICER is >$100 000/QALY but ≤$200 000/QALY. ICERs above the threshold of $200 000/QALY are shown in red. Horizontal lines represent the risk of measles exposure associated with travel to different international destinations. The base case (all pediatric international travelers) combination of 30 exposures/million travelers and 4 US-acquired cases per imported measles case is marked with an X. Abbreviations: PHE, pretravel health encounter; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; MMR, measles-mumps-rubella.

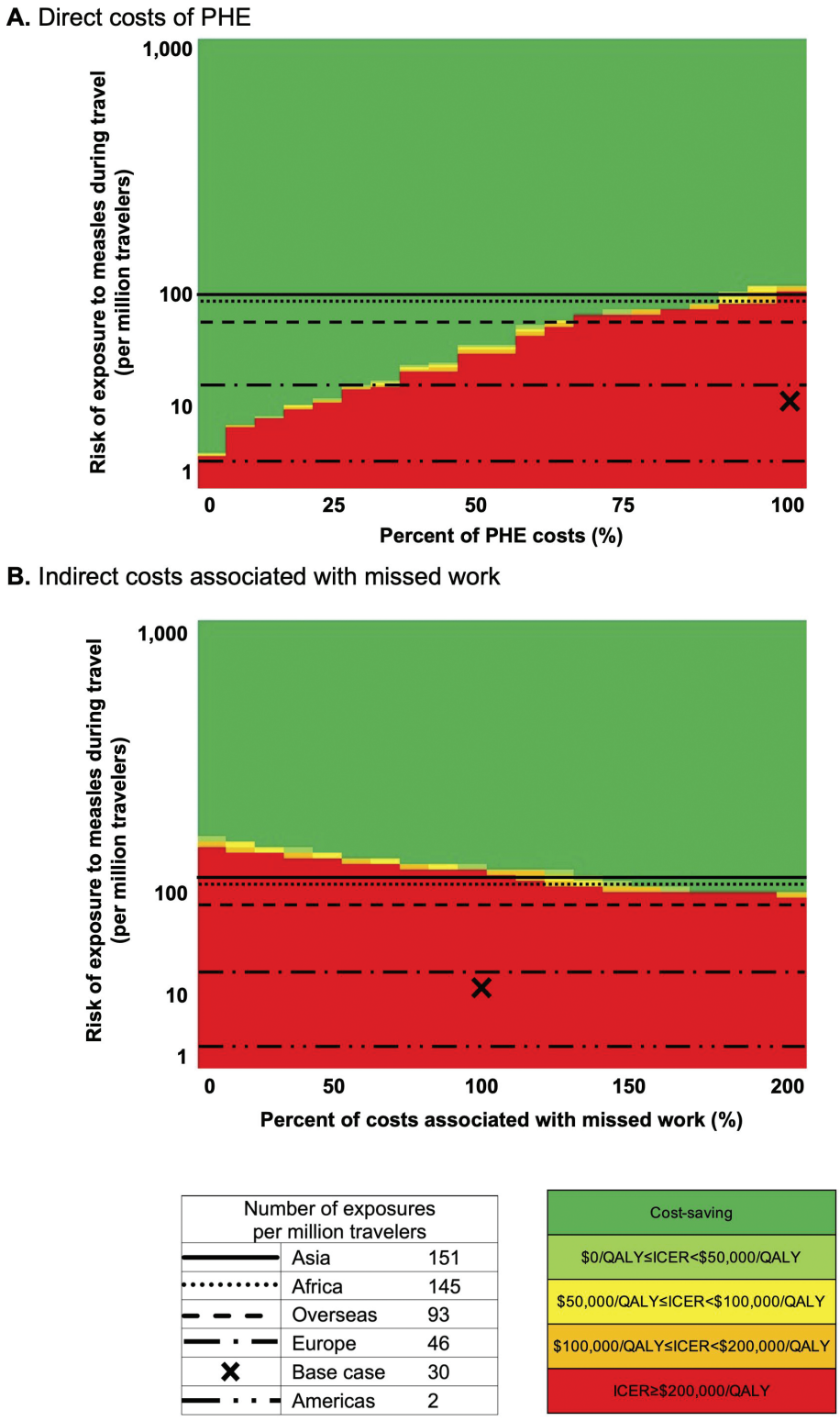
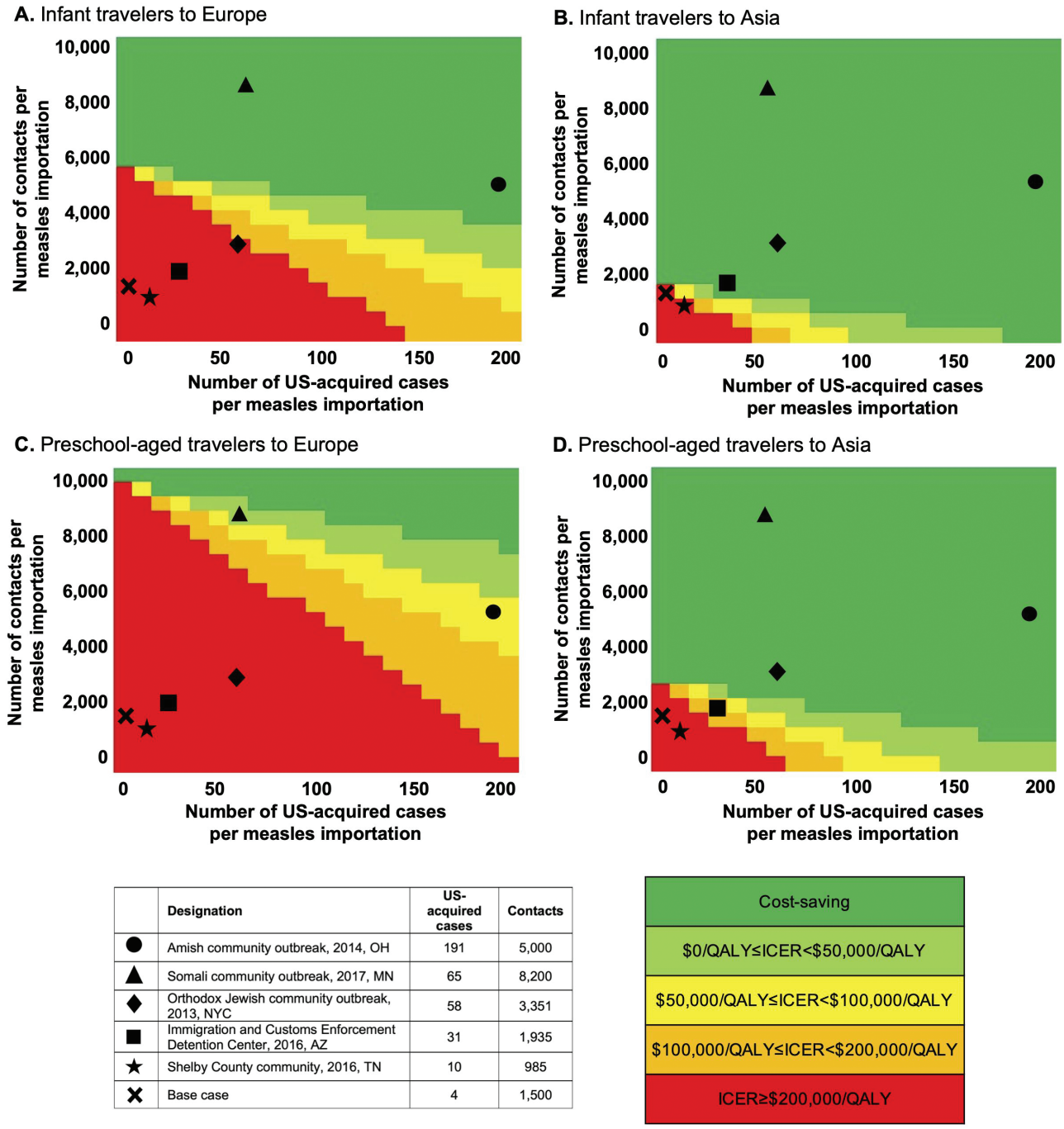


Figure 2. A 2-way sensitivity analysis depicts the value of PHE compared with no PHE for infant travelers when the risk of measles exposure and PHE direct costs (A) and indirect costs associated with missed work (B) are varied simultaneously. In this 2-way sensitivity analysis, the percent of base case costs is shown on the horizontal axis and the risk of exposure to measles during travel is shown on the vertical axis. Dark green marks when PHE is both clinically and economically preferred to no PHE (cost-saving); light green marks the values at which the ICER of PHE compared with no PHE is ≤$50 000/QALY; yellow marks the values at which the ICER is >$50 000/QALY but ≤$100 000/QALY; orange marks the values at which the ICER is >$100 000/QALY but ≤$200 000/QALY. ICERs above the threshold of $200 000/QALY are shown in red. Horizontal lines represent the risk of measles exposure associated with travel to different international destinations. The base case (all pediatric international travelers) combination of 30 exposures/million travelers and 100% of PHE direct costs is marked with an X. Abbreviations: PHE, pretravel health encounter; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; MMR, measles-mumps-rubella.



	Designation	US-acquired cases	Contacts
●	Amish community outbreak, 2014, OH	191	5,000
▲	Somali community outbreak, 2017, MN	65	8,200
◆	Orthodox Jewish community outbreak, 2013, NYC	58	3,351
■	Immigration and Customs Enforcement Detention Center, 2016, AZ	31	1,935
★	Shelby County community, 2016, TN	10	985
✖	Base case	4	1,500

Figure 3. Scenario analysis depicting the value of PHE compared with no PHE when pediatric travelers return from international travel to communities with low MMR vaccination coverage. Communities with low MMR vaccination coverage are vulnerable to outbreaks due to a measles importation, represented by more US-acquired cases (horizontal axis) and additional contacts (vertical axis). The value of PHE is plotted as the ICER resulting from each combination of these 2 parameters. Dark green marks when PHE is both clinically and economically preferred to no PHE (cost-saving); light green marks the values at which the ICER of PHE compared with no PHE is ≤$50 000/QALY; yellow marks the values at which the ICER is >$50 000/QALY but ≤$100 000/QALY; orange marks the values at which the ICER is >$100 000/QALY but ≤$200 000/QALY. ICERs above the threshold of $200 000/QALY are shown in red. The different panels depict the scenario analysis for infants travelers returning from Europe (A) or Asia (B) and preschool-aged travelers returning from Europe (C) or Asia (D). In each panel, the base case is denoted by an X (4 US-acquired cases per imported measles case and 1500 contacts); the other shapes represent the combinations of US-acquired cases and contacts associated with recent US outbreaks. Abbreviations: PHE, pretravel health encounter; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; MMR, measles-mumps-rubella.

in routine medical care from the widespread transmission of SARS-CoV-2, travelers and the communities to which they return may be less up to date on MMR and other childhood vaccinations [33]. Ensuring ACIP-recommended MMR vaccination for all eligible pediatric international travelers is thus particularly important now from a public health standpoint.

Our model-based results underscore that PHE would offer the greatest clinical benefit for infant travelers in terms of the number of measles cases averted per traveler, which supports current ACIP recommendations. From 2001 to 2016, children aged 6 to 11 months accounted for 15% of all internationally imported measles cases to the United States, which is disproportionately high given that infants comprise a small number of overall international travelers [26]. An early dose of MMR vaccination for infant travelers, who are likely to be unvaccinated, can reduce the probability of measles infection among exposed infants from 90% to 15% [1, 7], and our results underscore this clinical benefit. Because infants infected with measles are at high risk for severe disease and death, our analysis may underestimate the clinical benefits of pretravel MMR vaccination for infant travelers [2, 3].

Among preschool-aged travelers, PHE also offered the greatest clinical benefit when MMR vaccination was targeted to those departing for higher-risk destinations (eg, Africa and Asia). Since many preschool-aged children have already received 1 MMR vaccination [34, 35], the clinical benefits of PHE are less than for infants; the probability of acquiring measles after exposure decreases only from 7% to 3% for those given a second dose of MMR vaccination [7]. Although the absolute reduction in risk of measles infection after exposure will be less with the second MMR vaccination for preschool-aged travelers compared with a single MMR vaccination for infant travelers, more preschool-aged children are likely to travel internationally compared with infants. We assumed equal transmissibility among imported cases from infants and preschool travelers; if preschool-aged children transmit more efficiently [36], we would be underestimating the cost-effectiveness of PHE for this age group. Overall, PHE could have a larger public health impact in reducing measles importations when applied to preschool-aged travelers than infants.

Aside from protecting individual pediatric travelers, the other critical role of PHE is to prevent US outbreaks that can result from an imported measles case. Despite high national rates of childhood MMR vaccination, communities can be vulnerable to measles outbreaks due to vaccine hesitancy and nonmedical exemptions in schools [29, 30, 34, 35, 37]. In 2019, the United States reported 1282 measles cases, the greatest number since 1992 [38]; 8 of 22 outbreaks occurred in under-immunized, close-knit communities, accounting for 85% of all cases that year [38, 39]. We found that PHE has better value in settings where 1 measles importation results in many US-acquired cases and contacts [18, 22, 23]. Irrespective of the overall community to which an infected pediatric traveler returns, children aged 6 months to <6 years are likely to spend time in close proximity to children who might not yet be vaccinated, such as daycare centers or related settings. It is critical to avoid introducing measles into congregate settings with susceptible children, given its extreme contagiousness [40].

Although we evaluated the impact of a dedicated pretravel health encounter on screening for MMR eligibility and vaccination of eligible pediatric travelers with MMR, this could be achieved at a pediatrician's office. Infants visit their pediatrician frequently; thus, a well-child visit is likely to occur prior to international travel. If pediatricians identify children eligible for the travel-specific MMR recommendations during routine visits, this would further improve MMR uptake and value compared with no pretravel intervention, as demonstrated by our sensitivity analyses on improving vaccination acceptance and reducing PHE direct costs. To obtain the clinical benefits of ACIP recommendations for children, providers should take every opportunity to educate families about the risks of measles and encourage MMR vaccination among those eligible, despite past vaccination refusal and especially in the recent setting of fewer medical well-visits due to the coronavirus 2019 (COVID-19) pandemic [9, 33]. Discussing pretravel MMR vaccination at routine health visits may lead to the highest uptake, especially in communities with specific health-seeking behaviors and travel plans, and could be the most cost-effective approach if it achieves MMR vaccination for travelers at the highest risk for measles infection.

This analysis has limitations. Our estimated risk of measles exposure is likely an underestimate because not all measles cases are identified and reported to the CDC, and measles incidence has been rising; if so, PHE would be more cost-effective than our estimates. Although we used data from pediatric travelers attending GTEN sites to parameterize the model (who may demonstrate greater health-seeking behavior than the general population), our estimate of 92% coverage for ≥1 dose MMR for preschool-aged travelers is consistent with recent national data for children of similar ages [35]. We did not account for the additional benefits of immunity conferred by MMR vaccination against exposures to measles, mumps, or rubella within the United States, or additional health benefits for travelers from a pretravel health encounter. Vaccination has lifelong benefits that are not accounted for in our results based on a 1-time simulation of international travel. While our results do not explicitly quantify the benefit of PHE for under-immunized household contacts, we account for its ability to reduce transmissions after infected travelers return to communities with lower MMR vaccination coverage, which would include under-immunized families.

A pretravel health encounter to provide pediatric travelers ages 6 months to less than 6 years with MMR vaccination can reduce measles importations at a low cost per traveler. Although pretravel MMR vaccination can be cost-effective and even cost-saving if targeted to infant travelers to destinations with a high risk of measles exposure or returning to communities with low MMR vaccination coverage, this strategy has important clinical and public health benefits when deployed to all. Our results show that the best value is to vaccinate travelers from communities particularly vulnerable to measles outbreaks, but such travelers may be the least likely to accept vaccination given religious or personal beliefs. Therefore, MMR vaccination of eligible pediatric travelers should be

prioritized by healthcare providers at every opportunity. Given rising global measles incidence and extensive domestic measles outbreaks, it is critical to prioritize MMR vaccination for all eligible pediatric international travelers to reduce measles importations and outbreaks.

Supplementary Data

Supplementary materials are available at the *Journal of the Pediatric Infectious Diseases Society* online (http://jpids.oxfordjournals.org).

Notes

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Disclaimer. The findings, conclusions, and views expressed in this report are those of the author(s) and do not necessarily represent the official position of the Centers for Disease Control and Prevention/the Agency for Toxic Substances and Disease Registry, the U.S. Department of Health and Human Services, or the United States.

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